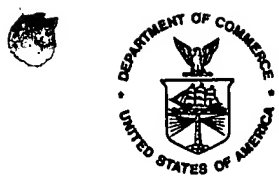

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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/224,558	12/30/98	SCHMIDT	A UP-6534

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EXAMINER	
NICKOL, G	
ART UNIT	**PAPER NUMBER**
1642	9

DATE MAILED: 08/01/00

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No.	Applicant(s)	
	09/224,558	SCHROIT, ALAN J.	
	Examiner	Art Unit	
	Gary B. Nickol Ph.D.	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).

Status

1)☐ Responsive to communication(s) filed on _____ .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-8,11,12 and 28-44* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-7,11,12 and 28-43* is/are rejected.

7)☒ Claim(s) *8,44* is/are objected to.

8)☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

a)☐ All b)☐ Some * c)☐ None of the CERTIFIED copies of the priority documents have been:

1.☐ received.

2.☐ received in Application No. (Series Code / Serial Number) _____ .

3.☐ received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. & 119(e).

Attachment(s)

15) ☒ Notice of References Cited (PTO-892)
16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
17) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *4-6* .
18) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
19) ☐ Notice of Informal Patent Application (PTO-152)
20) ☐ Other: .

DETAILED ACTION

Applicant's election without traverse filed May 8, 2000 (Paper No. 8) in response to the Office Action of March 29, 2000 is acknowledged and has been entered. Claims 1-8,11-12, and 28-44 are pending in the application. Claims 1-8,11-12, and 28-44 are currently under prosecution.

Allowable Subject Matter

Claims 8 and 44 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 11,39 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 11 is unclear for reciting "said lipid" in claim 7 because claim 7 recites lipid/polypeptide conjugate. Does "said lipid" refer to the lipid (Claim 1) or the lipid component of the lipid/polypeptide conjugate?

Claim 39 recites the limitation "said human" in claim 40. There is insufficient antecedent basis for this limitation.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-8,11-12,28-44 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of generating an immune response, inhibiting cancer cell growth or killing cancer cells with an immunologically effective amount of a phosphatidylserine/polylpeptide conjugate composition, does not reasonably provide enablement for a method of generating an immune response, inhibiting cancer cell growth or killing cancer cells with an immunologically effective amount of phosphatidylcholine or phosphatidylserine alone, and or a phosphatidylcholine/polypeptide conjugate composition. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

Factors to be considered in determining whether undue experimentation is required, are summarized in *Ex parte* Forman, 230 USPQ 546 (BPAI 1986). They include the nature of the

invention, the state of the prior art, the relative skill of those in the art, the amount of direction or guidance disclosed in the specification, the presence or absence of working examples, the predictability or unpredictability of the art, the breadth of the claims, and the quantity of experimentation which would be required in order to practice the invention as claimed.

The claims are broadly drawn to a method of inhibiting cancer cell growth or killing cancer cells comprising eliciting an immune response with an immunologically effective amount of a composition comprising a lipid or lipid/polypeptide conjugate (claim 1) wherein said lipid is phosphatidylcholine or phosphatidylserine (claim 11) or wherein said lipid or lipid/polypeptide conjugate is phosphatidylserine or a phosphatidylserine/polypetide conjugate (claim 28). The claims are further drawn to a method of generating an immune response, comprising administering to an animal a pharmaceutical composition comprising an immunologically effective amount of a phosphatidylcholine/polypeptide or a phosphatidylserine/polypeptide conjugate composition (claim 12) wherein said immune response is elicited with a lipid or lipid/polypeptide conjugate comprising a polypeptide selected from the group consisting of BSA, KLH,BGG, diphtheria toxin, and β2-glycoprotein I (claim 43).

This includes a method of generating an immune response, inhibiting cancer cell growth or killing cancer cells with an effective amount of a lipid wherein said lipid is phosphatidylcholine or phosphatidylserine. This also includes a method of generating an immune response, inhibiting cancer cell growth or killing cancer cells with an effective amount of a lipid/polypeptide conjugate wherein said lipid of the conjugate is phosphatidylcholine. The specification does not provide sufficient guidance or objective evidence to enable the invention as broadly claimed.

The specification teaches the inherent difficulty of generating an immune response against highly conserved lipids (page 3, line 16) wherein the preferred composition to generating such a response includes one or more lipid antigen compositions (page 7, lines 20-27). The specification further teaches that to achieve an immunologically effective formulation, it is desirable to administer a lipid-carrier conjugate composition (page 11, line 20). Further, phosphatidylserine is considered to be a non-immunogenic hapten and it is reasoned that an appropriate lipid-protein conjugate might elicit a potent and specific immune response (page 33, lines 28-30). Lastly, the specification provides no objective evidence that a lipid alone, including phosphatidylcholine or phosphatidylserine, will kill cancer cells, inhibit the growth of cancer cells, and or generate an immune response.

Thus, one cannot extrapolate the teachings of the specification to the scope of the claims because the claims are drawn to a method of generating an immune response, inhibiting cancer cell growth or killing cancer cells with a lipid alone, including phosphatidylcholine or phosphatidylserine. Based on the information in the specification, it would not be predictable that phosphatidylcholine or phosphatidylserine would alone, generate an immune response, inhibit cancer cell growth or kill cancer cells.

Further, the specification provides objective evidence that a phosphatidylcholine/polypeptide conjugate **does not** kill cancer cells, inhibit cancer cell growth or generate an immune response (Table 3, page 44) wherein control versus KLH-PC was not significant.

Thus, one cannot extrapolate the teachings of the specification to the scope of the claims because the claims include a method of generating an immune response, inhibiting cancer cell

growth or killing cancer cells with a phosphatidylcholine/polypeptide conjugate composition. And, based on the information in the specification, it would not be predictable that administration of a phosphatidylcholine/polypeptide conjugate would successfully generate an immune response, inhibit cancer cell growth or kill cancer cells.

Thus, since it is not possible to *predict*, based on the information in the specification, that the broadly claimed method will function as contemplated, it would require undue experimentation to one of skill in the art to practice the invention as claimed.

Claim Rejections - 35 USC § 102

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-6,11-12,28-42 are rejected under 35 U.S.C. 102(b) as being anticipated by Creaven, P. in (U.S. Patent No. 4,994,440, 1991, IDS) or (UCLA Symp. Mol. Cell. Biol, 1989, New Ser 89, pp. 297-303, meeting paper).

The claims are drawn to a method for inhibiting cancer cell growth or killing cancer cells comprising eliciting an immune response with an immunologically effective amount of a composition comprising a lipid or lipid/polypeptide conjugate (claim 1); wherein said cancer cell is a lymphoid, renal or bladder cancer cell (claim 2); wherein said cancer cell is comprised within an animal which has cancer or a tumor (claims 3,29,30); wherein said animal is a human and has cancer or a tumor (claims 4,31,32); wherein said composition comprises a pharmaceutical excipient (claim 5); wherein said composition is administered to said human

topically, parenterally, orally, subcutaneously, or by direct injection into a tissue site (claim 6); wherein said lipid is phosphatidylcholine or phosphatidylserine (claim 11); wherein said lipid or lipid/polypeptide conjugate is phosphatidylserine or a phosphatidylserine/polypeptide conjugate (claim 28);

The claims are further drawn to a method of generating an immune response, comprising administering to an animal a pharmaceutical composition comprising an immunologically effective amount of a phosphatidylcholine/polypeptide or a phosphatidylserine/polypeptide conjugate composition (claim 12); wherein said cancer cell is a lymphoid, renal or bladder cancer cell (claim 34) wherein said animal has a cancer or a tumor (claims 35-36); wherein said animal is a mouse (claim 40) or a rat, hamster, guinea pig or goat (claim 41) wherein said animal is a human and has cancer or a tumor (claims 37-39); wherein said composition is administered to said animal topically, parenterally, orally, subcutaneously, or by direct injection into a tissue site (claim 42).

Creaven teaches a method for inhibiting cancer cell growth or killing cancer cells comprising eliciting an immune response (Creaven, meeting abstract) with an immunologically effective amount of a composition comprising a lipid or lipid/polypeptide conjugate wherein said cancer cell is a renal cancer cell (abstract, and column 5, example 4); wherein said cancer cell is comprised within an animal which has cancer or a tumor; wherein said animal is a human and has cancer or a tumor; wherein said composition comprises a pharmaceutical excipient ; wherein said composition is administered to said human parenterally (column 2, lines 15-18); wherein said lipid of said lipid/polypeptide conjugate is phosphatidylcholine or phosphatidylserine ;

wherein said lipid or lipid/polypeptide conjugate is phosphatidylserine or a phosphatidylserine/polypeptide conjugate (column 2, lines 9-10).

Creaven further teaches a method of generating an immune response, comprising administering to an animal a pharmaceutical composition comprising an immunologically effective amount of a phosphatidylcholine/polypeptide or a phosphatidylserine/polypeptide conjugate composition (see meeting abstract); wherein said animal has a cancer or a tumor; wherein said animal is a human and has cancer or a tumor; wherein said composition is administered to said animal topically, parenterally, orally, subcutaneously, or by direct injection into a tissue site (column 2, lines 15-18). Although Creaven does not specifically teach the elicitation of an immune response in rats, hamsters, guinea pigs, or goats- the composition taught by Creaven is *effective* in mammals which includes humans, rats, hamsters, guinea pigs or goats.

Claims 1,5-6,11,28 are rejected under 35 U.S.C. 102(b) as being anticipated by Fidler et al (U.S. Patent No. 4,916,118, 1990, IDS).

The claims are drawn to a method for inhibiting cancer cell growth or killing cancer cells comprising eliciting an immune response with an immunologically effective amount of a composition comprising a lipid or lipid/polypeptide conjugate (claim 1); wherein said composition comprises a pharmaceutical excipient (claim 5); wherein said composition is administered to said human topically, parenterally, orally, subcutaneously, or by direct injection into a tissue site (claim 6); wherein said lipid is phosphatidylcholine or phosphatidylserine (claim 11); wherein said lipid or lipid/polypeptide conjugate is phosphatidylserine or a phosphatidylserine/polypeptide conjugate (claim 28);

Fidler et al. teach a method for inhibiting cancer cell growth or killing cancer cells comprising eliciting an immune response with an immunologically effective amount of a composition comprising a lipid or lipid/polypeptide conjugate (abstract); wherein said composition comprises a pharmaceutical excipient (column 9, line 4); wherein said composition is administered to said human parenterally and orally (bottom of column 8, top of column 9); wherein said lipid of said lipid/polypeptide conjugate is phosphatidylcholine or phosphatidylserine (abtract); wherein said lipid or lipid/polypeptide conjugate is phosphatidylserine or a phosphatidylserine/polypeptide conjugate (abstract).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-7,11-12,28-43 rejected under 35 U.S.C. 103(a) as being unpatentable over Creaven, P. in (U.S. Patent No. 4,994,440, 1991, IDS) and (UCLA Symp. Mol. Cell. Biol, 1989, New Ser 89, pp. 297-303, meeting paper) in view of Gupta et al (Vaccine, v13(14), 1995, pp. 1263-1276).

The claims are drawn to a method for inhibiting cancer cell growth or killing cancer cells comprising eliciting an immune response with an immunologically effective amount of a composition comprising a lipid or lipid/polypeptide conjugate (claim 1); wherein said cancer cell is a lymphoid, renal or bladder cancer cell (claim 2); wherein said cancer cell is comprised

within an animal which has cancer or a tumor (claims 3,29,30); wherein said animal is a human and has cancer or a tumor (claims 4,31,32,); wherein said composition comprises a pharmaceutical excipient (claim 5); wherein said composition is administered to said human topically, parenterally, orally, subcutaneously, or by direct injection into a tissue site (claim 6); wherein said immune response is elicited with lipid/polypeptide conjugate comprising a polypeptide selected from the group consisting of BSA, KLH, BGG, diptheria toxin, and β2-glycoprotein I (claim 7); wherein said lipid is phosphatidylcholine or phosphatidylserine (claim 11); wherein said lipid or lipid/polypeptide conjugate is phosphatidylserine or a phosphatidylserine/polypeptide conjugate (claim 28);

The claims are further drawn to a method of generating an immune response, comprising administering to an animal a pharmaceutical composition comprising an immunologically effective amount of a phosphatidylcholine/polypeptide or a phosphatidylserine/polypeptide conjugate composition (claim 12); wherein said animal comprises a cancer cell, has a cancer or a tumor (claims 33,35-36); wherein said cancer cell is a lymphoid, renal or bladder cancer cell (claim 34); wherein said animal is a mouse (claim 40) or a rat, hamster, guinea pig or goat (claim 41) wherein said animal is a human and has cancer or a tumor (claims 37-39); wherein said composition is administered to said animal topically, parenterally, orally, subcutaneously, or by direct injection into a tissue site (claim 42). wherein said immune response is elicited with lipid/polypeptide conjugate comprising a polypeptide selected from the group consisting of BSA, KLH, BGG, diptheria toxin, and β2-glycoprotein I (claim 43).

1. Creaven, P. teaches as set forth above.

2. Creaven, P. does not include the teachings of a vaccine comprising a polypeptide selected from the group consisting of BSA, KLH, BGG, diphtheria toxin, and β2-glycoprotein I in a rat, hamster, guinea pig or goat.
3. Gupta et al. teaches that the use of carrier proteins and or adjuvants, like diphtheria toxin, is well-established in the art for eliciting a higher immunogenic response (page 1269, 1st column, 2nd paragraph).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to modify the composition and methods of Creaven so as to include a polypeptide adjuvant such as diphtheria toxin as taught by Gupta et al. One would have been motivated to do so because the addition of adjuvants to vaccines is well-established in the art, and Gupta et al. teach that adjuvants, such as diptheria toxin, help antigen based vaccines to elicit an early, high, and long-lasting immune response with less antigen, thus saving on vaccine production costs (abstract).

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure. McNeil et al. (PNAS, 1990, v87, pp. 4120-4124, IDS) teach that foreign antigen complexed with β2-microglobin I could be the immunogenic stimulus for the production of aCL antibodies, these being a well-recognized occurrence in a number of infectious disease (page 4124, last paragraph).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gary B. Nickol Ph.D. whose telephone number is 703-305-7143. The examiner can normally be reached on M-F, 8:30-5:00 P.M..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony Caputa can be reached on 703-308-3995. The fax phone numbers for the organization where this application or proceeding is assigned are 703-305-3014 for regular communications and 703-308-4242 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Gary B. Nickol Ph.D.
Examiner
Art Unit 1642

GBN
July 31, 2000

ANTHONY C. CAPUTA
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